

59-A 38

HE 20.3035: 982

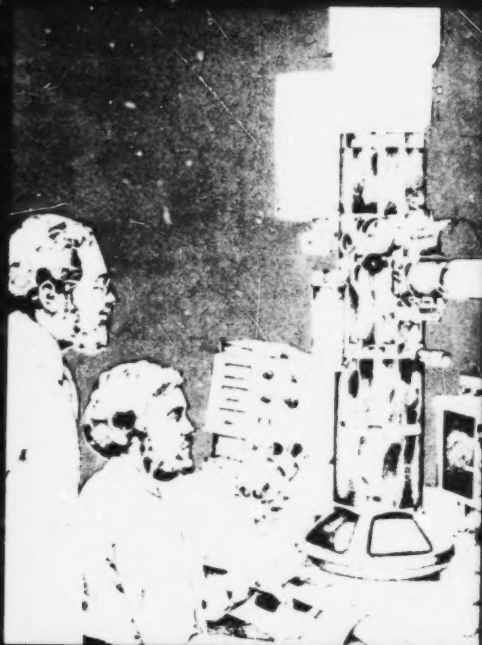
Division
of
Research
Services

Annual
Report

Fiscal
Year
1982

National
Institutes
of Health

COMPLETED



BEST COPY AVAILABLE

The Division of Research Services

The many specialized functions of the Division are designed to support all of the 18 Bureaus, Institutes, and Divisions (BIDs) which constitute the National Institutes of Health. The primary program emphasis, however, is directed at serving the 8,000 staff members of the intramural program, including more than 2,600 doctoral level scientists who conduct research in NIH laboratories.

Organizationally, the Division is structured to provide products and services in support of the sequential steps in every biomedical research project: planning, making available models and substrates, manipulating and measuring research materials, and recording and communicating research results.

- The Library Branch processes or has access to virtually all published biomedical knowledge to assist the investigator in planning and designing his/her project.
- The Veterinary Resources Branch provides the animal models, organic materials, and proper facilities for their use.
- The Biomedical Engineering and Instrumentation Branch collaborates with the investigator in devising the means whereby research materials may be manipulated and results measured, often with highly sophisticated electronic equipment.
- Finally, the skills of the Medical Arts and Photography Branch are available to all investigators to enable them to record and communicate the results of their research to the scientific community.

Service to NIH Research

Joe R. Held, D.V.M., Director
Division of Research Services
National Institutes of Health

All components of the National Institutes of Health faced a special challenge in Fiscal Year 1982: to keep up the high level of biomedical research performed or funded by NIH while also keeping costs within the limits required by tight budgets.

The management and staff of the Division of Research Services face the same challenge in their task of supplying vital services to NIH's intramural research programs. The following reports of the DRS Branches demonstrates how the Division is following through on its 26-year tradition of service to NIH research. A few introductory highlights from this year's activities might give the flavor of that service:

Biomedical Engineering and Instrumentation Branch

BEIB engineers and instrumentation specialists were particularly pleased this year when Neuro-PET—a vastly improved positron emission tomography scanner—was put into regular clinical use by investigators in the National Institute of Neurological and Communicative Diseases and Stroke (NINCDS). The new scanner, conceived by the NINCDS investigators, is named Neuro-PET for its ability to produce clearer, more precise pictures of the brain than previous PET scanners. BEIB staff in the Electrical Engineering Section, Mechanical Engineering Section, Research Instrumentation Section, and Mechanical Instrumentation Fabrication Section all shared in making NINCDS's improved diagnostic tool possible.

The quality of PET images depends largely on the efficient detection of gamma rays emitted in coincident pairs from the brain of a patient into whose bloodstream radioisotopes have been injected. For Neuro-PET, the NINCDS scientists designed a system of 512 crystal gamma ray detectors (many more than in standard PET scanners) packed tightly into four small-diameter rings.

BEIB engineers designed a sophisticated and complex electronics package for Neuro-PET that can identify coincident pulses from two simultaneous gamma rays among 40,960 possible pairs of detectors, and can code the pulses into numerical data to be transmitted to a computer.

BEIB engineers also designed a gantry to support the rings of detectors and a mechanical system for moving the rings in the desired pattern around the patient's head. These mechanisms were built by BEIB mechanical instrumentation fabricators, who also made valuable suggestions and performed the more detailed designing.

Work on Neuro-PET is not yet complete in NINCDS and BEIB. When it is fully operational, it will produce seven simultaneous brain-slice views, giving even more precision and speedier examinations.

Veterinary Resources Branch

The biomedical research community has become increasingly aware in recent years of the importance of genetic monitoring of inbred laboratory rodents. This awareness has been sharpened recently as journal articles discussed the possible invalidating effect of genetic contamination on research results. For example, a 1982 article in *ILAR News* (Institute of Laboratory Animal Resources) pointed out, "It is high time that all institutions and commercial breeders give serious thought to the development of genetic quality-assurance programs of the sort already implemented by several of the more progressive organizations." The DRS Veterinary Resources Branch inaugurated its Genetics Unit in 1977, both to monitor the genetic integrity of mice and rats maintained by the Branch and to respond to investigators' concerns about animals obtained from contractors. The Unit since then has steadily increased and refined its armamentarium of genetic profiles, using biochemical, immunological, and morphological markers to help investigators ensure the validity and comparability of research results.

Medical Arts and Photography Branch

Though MAPB is primarily engaged in helping researchers graphically record and communicate their findings, the Branch also meets a variety of other NIH information needs. One of their most challenging tasks in FY 1982 was to prepare, on very short notice, 18 exhibits for the White House Conference on Aging. Each exhibit had to focus on one NIH Bureau, Institute, or Division (BID), and illustrate that BID's contributions to improving the health of our nation's elderly. MAPB had the 18 exhibits completed and on display at the conference site when the participants arrived in Washington. But MAPB staff had also seen an opportunity to make double use of the exhibits and thereby help out the NIH components in a time of tight budgets. The Branch designers prepared the exhibits so that, with some modifications, they are now on view in a permanent site—the new NIH Information Center in the Ambulatory Care Research Facility (ACRF).

Library Branch

The NIH Library's portion of this report quite rightly focuses on the automated library services now being installed. But another development this year will also pay off in more efficient service to users: the Library came to grips with the problems of rapidly diminishing space. In the 15 years since the Library moved to its present site, the collection has more than doubled in size. The space crunch became painfully evident when Library staff were intermittently unable to shelve some materials.

One part of the solution is the move to microform. This year the Library accelerated its replacement of backfiles of less-used journals by microfilm versions, and also replaced its bulky collection of telephone books and college catalogs with microfiche.

The other part of the solution is more complex. Working closely with the Library Advisory Committee and other members of the NIH scientific community, the Library is evaluating its entire collection—journals and books—to perform a necessary winnowing without lessening its ability to respond to investigators' needs. The review is being performed in a way designed to give wide notice and review of all proposed removals.

Automated Data Processing in DRS

The large-scale automation of NIH Library services, now under way, is only one part of the Division's continuing increased use of automation to improve output and effectiveness on behalf of NIH intramural research. Growth, innovation, and adjustments in the use of resources are the expressions of an organization geared to meeting the needs of continually evolving research efforts.

In addition to the NIH Library's expanding system, DRS automated data processing systems already in operation include Small Animal Billing, Primate Inventory and Management, and Canine Colony Management in the Veterinary Resources Branch; Design Billing and Graphics Billing in the Medical Arts and Photography Branch; and Scientific Equipment Rental in the Biomedical Engineering and Instrumentation Branch. The Division is planning to purchase additional ADP equipment and software packages during the next five years for use in support of intramural research.

The NIH Library's online catalog and circulation control systems will be in operation around the end of FY 1983, to be followed by other library systems including accounting and management reports, cataloging support, and controls of acquisitions, serial publications, and inventory.

The Small Animal Scientific Data System, to be implemented in the Veterinary Resources Branch over the next five to seven years, will contribute strongly to laboratory animal management by collecting and maintaining comprehensive breeding, genetic, experimental, and environmental data. It will not only provide protocol management for experiments conducted within the DRS facilities, but will also furnish other investigators with fuller information for selecting the best animal models for particular research protocols.

Financial Operations

DRS's original FY 1982 budget authority of \$30,891,000 provided for a five percent increase from FY 1981 actual obligations. However, in a continuing effort to initiate cost saving measures, the Division was able to decrease its 1982 requirements by 8.4 percent. Reductions and cost saving methods were examined across the entire Division, with savings primarily in areas financed under the Service and Supply Fund in the Veterinary Resources Branch and the Medical Arts and Photography Branch.

The contract mechanism enabled the Division to adjust services and cost without adversely affecting the NIH. A study on the policies for acquiring commercial or industrial type products and services needed by the Government (OMB Circular A-76) was performed in the Veterinary Resources Branch, resulting in savings of \$75,000 from a contract for maintaining a nonhuman primate breeding colony. Another primate breeding colony was sold, eliminating \$300,000 obligations. The Medical Arts and Photography Branch initiated a bidding process for jobs going to contractors, insuring the best rate for the government. The current economic situation enhanced the success of this process, which contributed significantly to the \$1,018,000 savings.

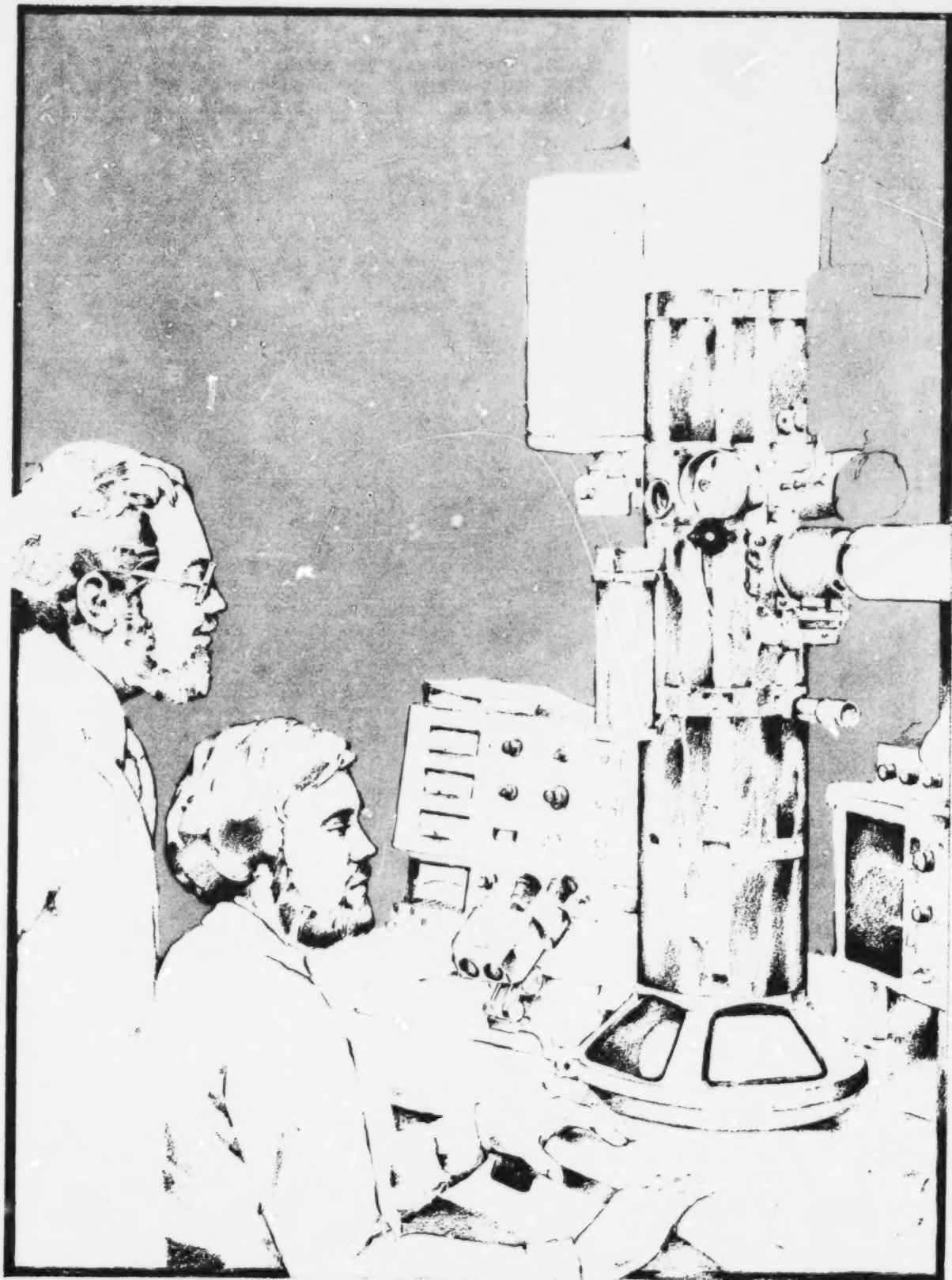
While faced with the challenge of operating under budget constraints, the Division continued to provide the high quality services to the NIH intramural program and meet increased demands, especially in the repair and maintenance of research instrumentation, primate holding, dog holding, and the purchase of additional equipment for the highly used Scientific Equipment Rental Program. The installation of a total Library automated system continued on schedule.

In the coming year the Division will continue to explore methods to increase productivity, reduce cost, and respond effectively to the NIH scientific community.

**Division of Research Services
Annual Budget
(in thousands of dollars)**

	FY-81	FY-82	Increase/ Savings
Veterinary Resources	\$12,999	\$12,534	\$ -465
Biomedical Engineering & Instrumentation	8,145	8,460	+ 315
Library	3,002	3,177	+ 175
Medical Arts & Photography	5,345	4,327	-1,018
Total	\$29,491	\$28,498	\$ -993

BEST COPY AVAILABLE



Biomedical Engineering and Instrumentation Branch

Murray Eden, Ph.D., Chief

Engineering and Physical Sciences for NIH Research

A reliable way to measure minute quantities of biologically important elements in tissues has been an elusive need of NIH's research community for many years. The Biomedical Engineering and Instrumentation Branch (BEIB), NIH's central focus of consultative and collaborative support for a wide variety of specialized skills in engineering and the physical sciences, is working to meet that need.

The approach centers upon a 200 KEV analytical electron microscope, specially adapted to produce map-like pictures of the distributions of chemical concentrations within tissues—in addition to the more traditional morphological images. When fully operational, the specially modified microscope will be capable of detecting certain elements in quantities as small as 10^{-20} gram with a spatial resolution under 10 nanometers.

The signals which the microscope produces for analysis are those of the characteristic x-rays and electron energy losses resulting from accelerated electrons interacting with core electrons of the specimen's atoms. In collaboration with the Division of Computer Research and Technology (DCRT), BEIB has interconnected a fast and relatively large "minicomputer" directly to the microscope to acquire these signals and produce the images.

The project's developmental phase is nearing completion, culminating 20 man-years of work over a four year period. Ten man-years have gone into development and modification of the instrumentation. Another ten, the work of the Computer Systems Laboratory, DCRT, have gone into producing the requisite software.

In work with the National Institute of Dental Research, BEIB has already successfully recorded preliminary energy loss images from ameloblasts (enamel-forming cells in the teeth), demonstrating significant amounts of calcium in the secretory granules. Use of such images should help achieve a better understanding of the function of ameloblasts in tooth enamel mineralization.

In other preliminary work with the microscope, measurements on fluorinated biological molecules indicate that some ring compounds (such as neurotransmitters) may be quite stable against radiation damage in the electron beam. BEIB plans to incorporate such substances into cells and to attempt imaging these components with the fluorine label.

In 1982, significant progress has also been made on another major imaging project—NMR imaging for use in medical diagnosis. In particular, BEIB has interconnected the system's spectrometer, pulse programmer, array processor, and computer and has successfully tested several developmental aspects of the system by producing a one-dimensional NMR image. Several other advances will lead to the production of images with information relating to three-dimensional structures.

In collaboration with the Surgical Neurology Branch of the National Institute of Neurology and Communicative Disorders and Stroke, BEIB has made operational an automated image quantification system that can determine the toxicity of chemotherapeutic agents on tumor cells. A concurrent project on an electron microscope has resulted in a five-to ten-fold increase in cell counting speed, as well as substantial improvements in statistical accuracy and numerical consistency. This study is continuing with the goal of improving understanding of brain cancer cell morphology.

The Branch has also been quite busy fulfilling its commitment to provide the NIH research community with a broad range of scientific and engineering expertise. For example, BEIB has collaborated in more than 200 projects to produce advanced instrumentation, models, methods, and techniques dedicated to the acquisition of biomedical information previously unavailable to NIH's scientists.

The staff of 40 professional physical scientists and engineers and 77 technical support personnel responded to over 3,100 requests for the fabrication and modification of laboratory devices and made another 8,600 repairs or minor changes of scientific equipment.

In addition, BEIB and the U.S. Agency for International Development have a continuing agreement in which BEIB provides technical assistance to less developed countries wishing to increase their ability to repair and maintain scientific and medical instrumentation. Currently, BEIB is working closely in this way with the government of Egypt and the governments of several Caribbean nations.

BEIB's professional staff function within four sections and the Office of the Chief. Here is a brief description of their activities in FY 1982:

Applied Clinical Engineering Section (ACES)

This multidisciplinary group, located in the Clinical Center/ACRF complex, provides diversified engineering expertise to a wide variety of collaborative efforts in basic and applied biomedical research. For example, the group is working with the Clinical Pharmacology Branch of the National Cancer Institute to develop a triple-laser flow cytometer that will enhance studies of cancer cell kinetics and hasten the evaluation of chemotherapeutic regimens. The group has also incorporated a PDP 11/34 minicomputer into the system to help the researchers more rapidly acquire and analyze clinical cell samples.

ACES is working in conjunction with Ortec Corporation to develop a concomitant device that will strengthen the results obtained from the flow cytometer. The auxiliary device is a TV-based, microscopic-image analyzer, intended to allow quantification of cellular DNA synthesis. The equipment will use a grain counting technique applicable to specially prepared autoradiographic specimens. ACES's primary contributions were in solving a grain overlay problem and in the analytical treatment of interference introduced by the presence of specific stains bound to the DNA.

Similarly, engineering concepts provided by the section are supporting a flow cytometer used by the National Institutes of Allergy and Infectious Diseases' Laboratory of Parasitic Diseases. The instrument's electronics have been significantly updated, thereby extending its applications. The laboratory is now able to delve more completely into biologic research concerned with the growth mechanisms of intracellular protozoan parasites.

Over the past year, the Laboratory of Animal Surgery of the National Heart, Lung and Blood Institute and the Applied Clinical Engineering Section have worked together to study the physiological principles underlying oscillometry—an old but newly revisited technique for measuring blood pressure indirectly. The method works through analysis of the pulse pattern of pressure changes in a blood pressure cuff during its deflation cycle. Because the technique requires no external transducers and is easy to apply, oscillometry is well suited to indirect measurements of blood pressure in research animals.

On the basis of an *in vitro* oscillometric model and studies using laboratory dogs, the members of the Applied Clinical Engineering Section have identified several underlying principles involving the rheology of arteries and the thermodynamic properties of the cuff. They are currently designing an oscillometric blood pressure system based upon these principles.

Collaboration with the National Heart, Lung and Blood Institute's Surgery Branch has resulted in a heart perfusion circuit that circulates a buffered analog of blood through an isolated heart. This device permits investigation of the heart's biochemical and physiological parameters. The system also allows investigators to induce temporary cardioplegia, during which certain pharmacologic agents can be introduced into the heart. The scientists can then assess the ability of the drugs to maintain cellular life by comparing the heart's pre- and postplegic pumping abilities. This technique may have some utility in stopping and restarting the heart during cardiac surgery and may therefore simplify certain open-heart surgical procedures.

The opening of the Clinical Center's new Ambulatory Care Research Facility (ACRF) led to several new areas of collaborative research for ACES. A completely new speech pathology lab within the ACRF has created a need for specially modified ultrasound equipment to be used in the diagnosis and rehabilitation of certain speech impairments. Similarly, ACES is collaborating with the Diagnostic Radiology Branch of the Clinical Center in developing a miniature, overhead TV camera system to permit precise monitoring of nuclear diagnostic studies during surgical procedures.

ACES is also providing the clinical engineering support necessary for the 500-bed Clinical Center and the Ambulatory Care Research Facility (ACRF). This role evolved from the electrical safety program established for patient care equipment. It consists of programs in the areas of technical standards, medical equipment management, and the training of medical and support staff. An example of this is the section's participation in the formulation and modification of standards affecting patient care.

Chemical Engineering Section (CES)

Historically, chemical engineering developed as a discipline to facilitate the analysis, design, and control of large-scale chemical plants in which intrinsic chemical events are associated with various physical processes such as flow, mixing, and transport. The methodologies of this discipline form a natural and clearly delineated body of science and practice applicable to many biological problems in which physical processes influence biochemical interactions or even dominate them.

The Chemical Engineering Section has pioneered in the development of physiological pharmacokinetics and continues to service as a resource for the design and interpretation of laboratory and clinical studies involving the discipline. Recent work has included the development of pharmacokinetic models for a variety of anticancer drugs, radiation sensitizers, and environmental contaminants. The section has placed particular emphasis on the development of a protocol for the quantitative use of pharmacokinetics in mice and man to improve the effectiveness of Phase I clinical trials. In addition, CES has advanced pharmacokinetic theory through the development of mathematical models, including some for the diffusion of drugs into tissues from body cavities such as the peritoneal or cerebrospinal fluid spaces. These distributed models provide considerable insight into the factors affecting drug absorption and the shape of the concentration profiles in tissues.

A collaboration with the Food and Drug Administration and the American Red Cross, begun during the year, is developing improved techniques for the study of cells in culture. This collaboration builds on the section's past experience with cell culture and synthetic membrane technology, including the application of principles of fluid mechanics and mass transport to the design of new instruments for studying

cells under carefully controlled conditions. One instrument permits simultaneous visual and electrical observations of cultured toad bladder epithelium. A second allows study of the morphology and physiology of arterial endothelial cells exposed to various fluid shear stresses. The devices allow for the regulation of the chemical environment of the cells and can be used to test cellular interactions with well-characterized synthetic support materials.

Analysis of the amino acid sequence of proteins is becoming an increasingly important element in biomedical research. In collaboration with the National Cancer Institute, CES is seeking improved methods for automated sequencing of amino acids. One approach involves the modification of commercially available instruments to enhance the reproducibility and the yield of the sequencing process. The section is also pursuing new technologies to improve techniques for easy, inexpensive, and reliable analysis of very small amounts of proteins and peptides. One new approach involves the use of ultrafiltration membranes that will serve as reaction chamber and separation devices for removing products from reactants in the sequential degradation of the protein.

Development of a fiber-optic sensor for measurements of blood and tissue oxygen pressure has resulted in a working system of probe and associated instrumentation. Evaluation and development for their practical application are under way. The small size, safety, reliability, and low cost of such a probe should provide a significant improvement over currently available methods. The probe is modeled after a similar fiber-optic probe for pH measurement, previously developed in CES and modified and further developed by BEIB's Mechanical Engineering Section for use in physiological experiments. These optical sensors are based on dye-indicator principles with specificity achieved by chemical means.

Segmented polyurethane continues to be an important elastomeric material for applications in surgical implants such as artificial-heart assist pumps, total artificial hearts, and insulation for neuro- and cardiac electrodes. Long term *in vitro* studies, carried out in the CES laboratory for periods up to 13½ years, have elucidated many of the physical characteristics of this polymer when

it is subjected to storage under various wet and dry conditions. Photomicrographic and scanning electron micrographic analyses have disclosed discontinuities in the physical and chemical structure of the polymer that have been attributed to causes arising during synthesis, subsequent handling, and fabrication. These variances may be significant to problems of blood compatibility and surface calcification. CES is also continuing work on the development of special purpose catheters for therapeutic applications. Among these are a balloon catheter for treating bladder tumors with radiation and a miniature flow-directed catheter for interventional radiology.

Electrical and Electronic Engineering Section (EEES)

The Electrical and Electronic Engineering Section continued development of a diverse range of custom instrumentation in support of NIH's intramural research. Despite the severe resource constraints affecting all of NIH, the group was able to increase its effectiveness through increased use of computer-aided design (CAD) and refinement of its interdisciplinary team approach. For example, new staff with expertise in biophysics and electro-optics are complementing the expertise of the section's specialists in electronics, micro-processors, and software.

The fruits of this approach are well exemplified by a new instrument that provides noninvasive measurement of the viability of platelets in transfusion bags. Through CAD, the group developed a sophisticated laser optical measurement technique that extracts the desired parameters by means of a microprocessor-based data handling system. No apparatus to make this important measurement had been developed previously.

A major project in collaboration with the National Institute of Neurological and Communicative Disorders and Stroke is approaching completion. The Neuro-PET scanner is already in regular clinical use, although its ultimate capability of yielding 7 slices is not yet fully implemented. Its electronic circuitry, developed by EEES, has contributed to achieving sensitivity and resolution higher than that of any commercially available instrument. (This project and the noninvasive platelet analyzer have also been supported by BEIB's Mechanical Engineering Section.)

The section has applied considerable effort to a variety of video systems, including some in which the TV camera tube (vidicon) is operated under highly abnormal conditions. A new technique that EEES developed for linearizing vidicon performance under such conditions is being used to good advantage in several spectroscopic applications.

The group also increased its emphasis on bus-oriented instrumentation systems. The expertise of EEES, coupled with the stock of bus-compatible instruments in BEIB's Scientific Equipment Rental Program, provides a unique capability for the rapid and economical development of sophisticated one-of-a-kind instrumentation systems.

A wide variety of other electronic instruments was also developed, ranging from data acquisition systems, controllers, and interfaces to more complex developments such as scanning and de-scanning systems for analytical electron microscopes.

Mechanical Engineering Section (MES)

The Mechanical Engineering Section conducted a wide variety of projects this year involving hardware development, as well as analytical and experimental studies. Several long term projects were brought to fruition, and a number of new initiatives were begun.

Several years of work on a miniature fiber optic pH probe have culminated in the development of a computerized five-channel instrument for measurements in canine myocardium. The National Heart, Lung and Blood Institute uses the instrument extensively as a vital part of several experiments on calcium antagonist drugs. The probe fits inside a 1/2 mm diameter needle and is extremely rugged and reliable; it is stable and accurate to less than 0.01 pH units. MES has improved the optical design so that an LED can provide the illumination, instead of the previously required tungsten light source driven by a high current stabilized DC supply.

In collaboration with NHLBI, the section has combined a microscope, micromanipulators, and a TV video system to study the mechanical properties of single red blood cell membranes. With this combination, both static deformations and time dependent deformations can be measured under prescribed loads to determine the shear moduli and viscosities of the membranes of normal and diseased red blood cells. MES will use the technique to study sickle cells at various oxygenation levels, and also the red blood cells of diabetics.

The section also developed an analytical continuum model of the left ventricle of the heart to aid in understanding myocardial function. Particular attention was given to the anisotropic effects resulting from the fiber orientations in the heart. The ventricular cycle was analyzed by

specifying the pressures at which the aortic and mitral valves open and close. Ejection fraction and other important parameters are calculated in closed form as functions of variables such as wall thickness, fiber angles, and muscle parameters.

Work continued on the miniature toposcopic catheter that has been under development for several years. The system's reliability and performance have been significantly improved, and clinical use is anticipated in the near future. The outer introducing catheter is number 7 French, and the everting element is 1½ mm in diameter (4.5 French).

During the past year MES has collaboratively collected a large quantity of experimental data on the uptake of fluorescein in tumors, using an *in vivo* fiber optic micro-fluorimetry system developed by members of the section. To analyze data, fast Fourier transform techniques are used to perform deconvolutions which reveal the transport characteristics of the tumors for markers with a range of molecular weights.

Another system being developed in MES is collaboration with the National Heart, Lung and Blood Institute (NHLBI) will allow more precise results in testing drugs used in cardiology. This is a servo pressure feedback control system, designed to control the aortic blood pressure in a dog on a phasic basis. It will eliminate downstream load pressure changes that have heretofore influenced results when the contractility effects of various drugs are being evaluated. Phasic pressure recorded before the drug intervention provides the servo's reference pressure for use after the intervention.

MES is also participating in a long term project with the National Cancer Institute and the Bureau of Radiological Health, FDA, involving the use of microwave radiation to produce localized hyperthermia for treatment of cervical cancer. This involves five steps: characterization of a specially procured microwave antenna system, any necessary modification of the antenna, performance of heat transfer analysis to predict temperature profiles as a function of radiation and perfusion, phantom studies, and collaboration with NCI clinicians to determine doses. If the results justify further elaboration, we will ultimately develop a completely computerized system that would account for factors such as variations in anatomy.

Analytical Methods Group (AMG)

This group within the Office of the Chief collaborates with NIH investigators in three major areas: (1) trace element and complex species characterization and quantitation, (2) mass spectrometry, and (3) analytical ultracentrifugation.

Increasingly sensitive methods of analysis are clarifying the significance of trace elements and their complex species within organisms, especially their relationship to disease processes. This research requires identification, characterization, and quantitation of several elements (for example, copper and gallium) and numerous transition metals (including iron, vanadium, manganese, cobalt, and platinum) and their complex species in biological tissues and fluids. Sensitive analytical techniques are applicable to the study of such things as enzyme inhibitors in affective disorders, enzyme activators in heart disease, the formulation of improved anti-tumor drugs, and pharmacokinetic modeling. As an example, platinum (positively identified by its x-ray energy) is found concentrated in lysosomes of renal cells of rats treated with the antitumor drug cis-Platin. Work is also continuing on development of techniques of administration that minimize the toxic effects of this drug on the kidney. We are doing this by adjusting the proportions of the several chemical forms containing platinum in the drug formulations.

A Secondary Emission Mass Spectrometer (SEMS) system is being assembled to study particle-induced ionization of biological and high molecular weight compounds. The instrument will also serve as a test facility for the development of ion sources and guns for the mass spectrometers used in NIH intramural studies. Other activities have included development of cold emitters for ion sources and modification of mass spectrometers on the NIH campus for application of particle ionization bombardment.

The group has also developed a method of determining the resolving power of low resolution mass spectrometers. Reference compounds used in this method can be used to test the sensitivity of quadrupole mass spectrometers in a high mass range. The group has also built a special quadrupole RF power supply to drive the QUISTOR, which will be studied for possible application in analytical mass spectrometry.

Analytical ultracentrifugation studies have led to collaborative publications on several subjects: the self-association of myoglobin at physiological concentrations, the molecular weight distributions of polysaccharide from *E. coli*, and the thermodynamics of self-association of the C-II protein of phage. Our principal ongoing studies of associating systems are on the stoichiometry and association constants for the binding of plasminogen to fibrinogen.

The group expects to give particular emphasis to investigating the thermodynamics of interaction of various proteins involved in blood clotting in order to identify the interacting molecular regions and their relation to clotting mechanisms.

Scientific Equipment Services (SES)

This group continues to provide scientific equipment design, fabrication, repair and rental services to the NIH scientific community. FY 1982 has brought a noticeable increase in repair requests and a decrease in fabrication requests.

The loss of three highly skilled repair technicians has compounded the effect of the increased repair workload. Because suitable replacements for these personnel have not been available, SES has initiated a formal apprentice program in equipment repair. Three persons are currently enrolled; their training will last between three and four years. During the first year the students are enrolled for 16 hours per week in an electronics technology program at a local school. This training is supplemented by on-the-job training and formal short term courses in other areas, such as refrigeration. To date, we are encouraged with the progress made by the trainees and anticipate that additional trainees will be added when other employees leave and qualified technicians cannot be obtained.

SES management is continually reviewing its operation and attempting to initiate changes that will increase its efficiency.

The size of the Scientific Equipment Rental Program and its use by the NIH scientific community are both continuing to grow. During FY 1982 SES purchased an additional \$1,500,000 worth of equipment, bringing the value of the equipment in the program to \$6,000,000.

Outlook for FY 1983

In the coming year the Applied Clinical Engineering Section expects to continue its support of flow cytometry for both the National Cancer Institute and the National Institute of Arthritis, Diabetes, & Digestive & Kidney Diseases (NIADDKD). The opening of the ACRF is expected to create additional responsibilities for ACES, including assistance in setting up a new speech pathology laboratory.

The efforts of the Clinical Engineering Section in 1983 will be in several areas. One area of continuing emphasis will be pharmacokinetic modeling. Here, projects of direct clinical

significance are progressing, including the development of distributed models of both peritoneal and blood-brain transport of numerous anticancer drugs, such as cis-Platin and 5-fluorouracil. An area that is emerging with particular interest is the application of principles of chemical engineering to improvements in instrumentation and techniques of biological measurement. Projects in this area will include development of an implantable fiber optic pH and pO₂ probe, investigation of a novel ultrafiltration-based reactor for protein sequencing, and the design of membrane-based sampling systems for *in vivo* and *in vitro* kinetic studies. CES will also seek more compatible and more durable biomaterials for such implants as heart valves and catheters, and the section expects to apply its previous experiences with hemodynamic studies to new studies of the effects of fluid shear on cultured endothelial cells as these phenomena relate to the development of atherosclerosis.

The Electrical and Electronic Engineering Section plans to emphasize new applications of electro-optical technologies to further developments in the area of bus oriented systems and to support the normal requests for new or modified instrumentation. EEES will also apply considerable effort to completing several major recent projects, including the Neuro-PET, custom electronics for the BEIB electron microscope facility, and the instrument for quantifying platelet viability.

In the Mechanical Engineering Section, a major initiative is beginning in localized hyperthermia, using microwave energy as an adjunct to cancer chemotherapy. The section will also emphasize theoretical biomechanics of soft tissues (e.g., arteries, the myocardium, and other muscles), and experimental studies of the properties of red cell membranes. The toposcopic catheter system will be used clinically, and MES anticipates that numerous laboratories within NIH will use an inexpensive version of the BEIB-developed fiber-optic pH probe. Moreover, novel instrumentation and control for experiments in cardiology that are currently under development (such as phasic aortic pressure control) will receive their first tests.

As developmental work on the instrumentation and software of BEIB's analytical electron microscope comes to a close, the Branch anticipates a number of new collaborations on important biological problems. In analytical methods, BEIB will extend and refine work on the techniques for quantitation and speciation of metal complexes and study their interactions in biological systems. The effort in mass spectrometry will be on testing and evaluation of the equipment and development of data processing methods with application to new systems. In analytical ultracentrifugation further improvements are planned in the data acquisition system with application to thermodynamic measurements on biological macromolecules.

BEIB also expects to have satisfactorily researched and built the basic instrumentation of the NMR imager in 1983 and to have obtained high quality images. More emphasis will be placed on the developing of new NMR imaging techniques with a view to obtaining information on flow, diffusion, and metabolism as well as the more common parameters of relaxation times and proton density. New techniques for displaying the information (involving the use of color) will be under investigation, as will a variety of pulse sequences designed to compensate for inadequacies in field homogeneity.



Medical Arts and Photography Branch

Ronald B. Winterrowd, Chief

Graphic Arts in the Service of Research

Most of the Medical Arts and Photography Branch's work consists of documenting NIH investigators' scientific data through photographs and graphic illustrations for publication in journals or for presentation at scientific or lay meetings. MAPB also supplies various other NIH information needs.

The last ten years have seen an annual increase of from 10 to 20 percent in the Branch's graphic art services provided to the NIH community. In FY 1982, for the first time, the demand for these services did not rise, and in some sections it decreased. Inflation, budget constraints, and a moratorium on the printing of Federal publications contributed to the lessened demand. Fortunately, the large increases of the past several years were managed through an increased use of contractors, so it has been possible to absorb the current decreases without disrupting the inhouse program.

The Branch's staff of 49 artists, photographers, and other specialists has extensive expertise in converting data into effective presentations. They are highly skilled in meeting the needs of scientists for graphic presentation, medical arts, and still and motion picture photography, including photomacrography and photomicrography. Services include design and production of publications; preparation of slides, vugraphs, and other projected visual aids; animation artwork; technical, general, and medical illustrations; exhibit design; statistical drafting; display charts; posters; and medical models.

The philosophy of the Branch is to provide high quality professional services competitive in cost with commercially obtainable services. On contracted work, the staff works closely with vendors of graphic and photographic services to ensure that MAPB's quality standards are kept.

To reduce users' costs while maintaining productivity and product quality, MAPB has set up an educational program on cost awareness and cost reduction within the NIH community. It stresses the savings in money and time that investigators can derive by thinking through in advance how they want their articles and presentations illustrated, discussing their requirements with MAPB at an early stage, and adhering to their plan once it has been made.

Investigators are advised to submit complete, clear, and accurate raw data for display as early as possible. Careful planning can eliminate two causes of expense: 24-hour rush service to meet a deadline, and changes in artwork that has been prepared in final form. Rush service costs 50 to 100 percent more than regular, and changes or corrections on final artwork can double its cost.

Staff members also ask investigators to order only the necessary number of slides and pictures, and tell how to protect artwork for future reprinting; replacement of damaged materials can be as costly as the original.

In another effort to contain costs, the Graphics Unit requires bids on all contract work, even through procurement regulations require negotiations only for bids over \$500.00. This procedure has realized savings of approximately 25 percent.

Photography Section

The Photography Section's requests for services dropped by 9 percent during the year. Photography support services in photomicrography, photomacrography laboratory work, and technical information were provided to NIH investigators by highly trained photography technicians using advanced printing and processing equipment. To supplement our inhouse facilities, the section continued to obtain the services of vendors in the Washington, D.C., area.

Motion Picture Section

The number of filming requests was about the same as in 1981, with several more formal productions completed than in the previous year.

Design/Graphics Section

As a result of budget limitations and the moratorium on printing, the workload of the Design and Graphics Units decreased by 18 and 12 percent, respectively. Despite restrictions on costs, the sections' quality and performance standards remained high. This section, capable of filling requests for complex visual productions, received several awards during the year.

Medical Illustration Section

This section is staffed with talented, highly trained artists who possess a broad background in medical science. Their workload remained constant, with a trend toward surgical illustrations for journal articles and other scientific papers, slides, medical atlases, and other longer-term projects.

Outlook for FY 1983

Tight budgets will probably continue to hold down requests for the Branch's services. Because MAPB provides the vital function of recording and communicating the research findings of the NIH biomedical community, the Branch plans to continue aggressively finding and using new ways to reduce costs and improve services. The educational program to inform MAPB's clients how best to achieve their objectives will be continued.



Veterinary Resources Branch

Robert A. Whitney, D.V.M., Chief

Laboratory Animal Science—A Full Range of Services

The Veterinary Resources Branch (VRB) provides the NIH intramural research programs with a wide range of professional and technical services:

- Production of defined research animals
- Procurement, quarantine, conditioning, and issuance of animals from outside sources
- Management of a central animal surgery and radiology facility
- Animal disease diagnosis and control
- Genetic monitoring of defined research animals
- Research holding for primates, cats, dogs, and livestock
- Consultative services on animal health, care, husbandry, genetics, and nutrition.

VRB also maintains the NIH Animal Genetic Resource and provides administrative support for the Interagency Primate Steering Committee.

During FY 1982 the demand for research animals decreased somewhat, and one of VRB's major emphases has been to adjust the balance between supply and demand and to hold down costs.

The Branch's role as a public information source was intensified because of a high level of public interest in laboratory animals. By request of a Maryland court, VRB provided long-term care for several monkeys pending the outcome of trials and appeals concerning the maintenance of these research animals at a grantee institution. In addition, VRB staff members have been active on several NIH committees formed to address issues of animal care in intramural and extramural programs.

Animal Center Section

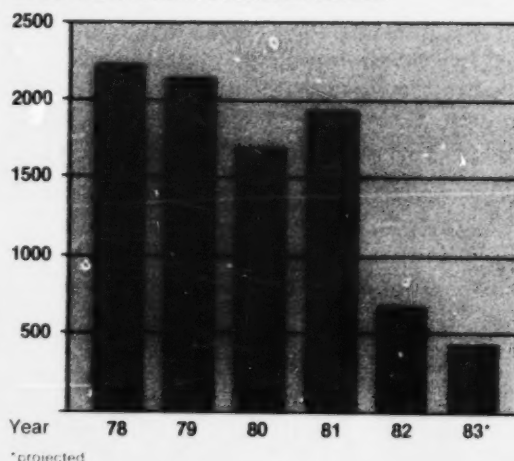
The NIH Animal Center in Poolesville, Maryland, produces and maintains large laboratory animals and provides related services and products for NIH investigators.

The Primate Quarantine Unit procures and quarantines nonhuman primates, manages contract breeding programs, and provides long-term holding of primates for NIH intramural research components and some other Federal research organizations.

The number of rhesus and cynomolgus monkeys issued has declined markedly, largely because of reduced requirements of the National Center for Drugs and Biologics (NCDB) of the Food and Drug Administration (Figure 1). On the other hand, research requiring monkeys has become more long-term in nature, and the Center's facilities are increasingly used to provide extended holding of primates for various institutes (Figure 2). In addition, one contract production program was terminated and the production level of another was reduced to avoid generating surplus rhesus monkeys. An interagency agreement was implemented to produce tamarins (*Saguinus mystax*) for NCDB research programs.

Livestock populations maintained by the Ungulate Unit remained stable (Figure 3), although the use of blood and blood products declined slightly. A herd of 225 miniature swine is maintained for the National Cancer Institute as a resource for studies in transportation immunology. In addition, stock was provided to a contractor to supplement production by the Animal Center. The National Heart, Lung, and Blood Institute increased its use of sheep for

Figure 1.
Total Nonhuman Primates Issued



surgical research, resulting in a greater demand for sheep blood and a greater number of sheep held pre- and postoperatively.

In the Carnivore Unit, programs are being modified to reflect marked curtailments in the demand for cats, foxhounds, and canine blood. Colony sizes have been reduced, and space is being converted to meet increased long-term holding requirements and to produce defined beagles for the National Cancer Institute (Figures 4 and 5).

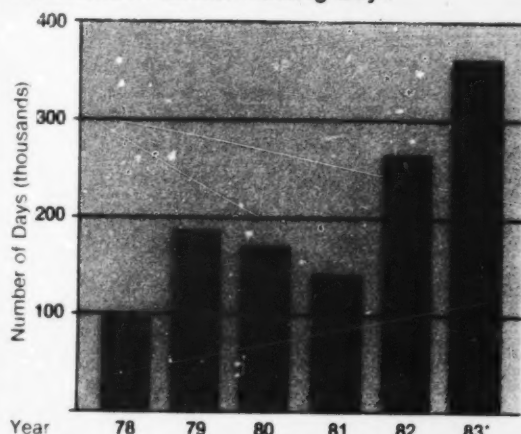
Small Animal Section

The Small Animal Section provides rodents and rabbits from its production colonies and also manages contracts for this purpose. It manages

the NIH Animal Genetic Resource, containing more than 200 defined strains, and has programs devoted to animal model development, nutrition, and health.

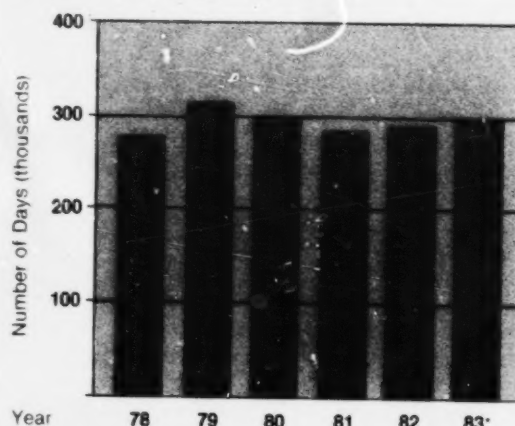
Approximately 230,000 animals were issued from the sections' colonies, a decline of 50,000 from last year, while the number obtained from contract sources was stable at 610,000 (Figure 6). The reduction was related to a decreased demand by NIH investigators and the need to halt production of some stocks and strains contaminated with mouse hepatitis virus until one autoclave was repaired. No new contracts for the purchase

Figure 2.
Nonhuman Primate Holding Days



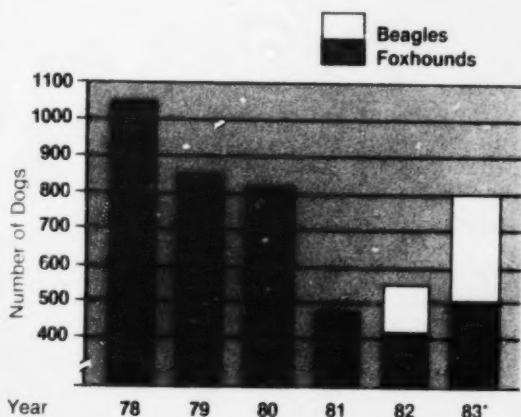
*projected

Figure 3.
Livestock Holding Days



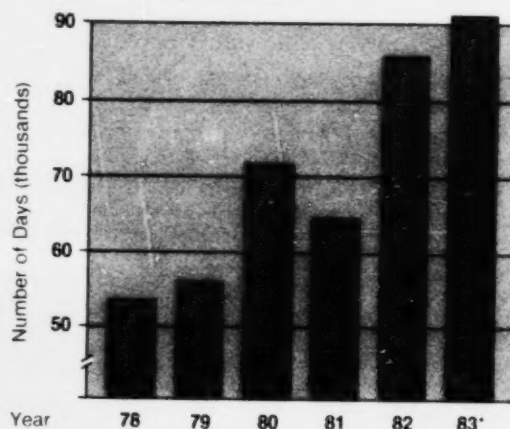
*projected

Figure 4.
Foxhounds and Beagles Issued



*projected

Figure 5.
Long-term Dog Holding



*projected

of small animals from commercial breeders were issued during the year.

Because of investigators' concern with the potential effects of diet on experimental results, many of them requested nutritional information or modifications in diet formulations to accommodate specific program requirements. The program to monitor diets for various chemical contaminants continues, but there is no indication so far that contaminants are a problem when diets are manufactured in facilities that meet NIH contract requirements.

The development of new open formula diets continues, with emphasis on a nonhuman primate diet and a rodent diet formulated specifically for use in toxicology studies. The nonhuman primate diet has been evaluated in various colonies and will apparently soon replace the closed formula diet currently purchased by sole-source contract. A price evaluation showed that open formula diets purchased through advertised contracts cost the NIH about 38 percent less than closed formula diets purchased as sole-source items. It is estimated the NIH will save about \$80,000 this year by using open formula diets.

Extensive studies have been undertaken in collaboration with the National Heart, Lung, and Blood Institute and the National Eye Institute to ascertain the effects of dietary constituents on the incidence of stroke in the stroke-prone rat and the incidence of cataracts in PETH and RCS rats.

Renovations completed in July will allow VRB, for the first time, to offer a rodent holding service for NIH investigators. The renovated facilities will be used initially to hold animals for the National Institute of Allergy and Infectious Diseases until

renovations of that institute's facilities are completed.

Comparative Pathology Section

The Comparative Pathology Section is responsible for monitoring the health status of laboratory animals produced, quarantined, or used at the NIH. It studies the naturally occurring diseases of these animals and develops measures to improve their health. The section also ensures the genetic quality of animals produced by VRB either for use by NIH programs or to be sent throughout the world from the NIH Animal Genetic Resource.

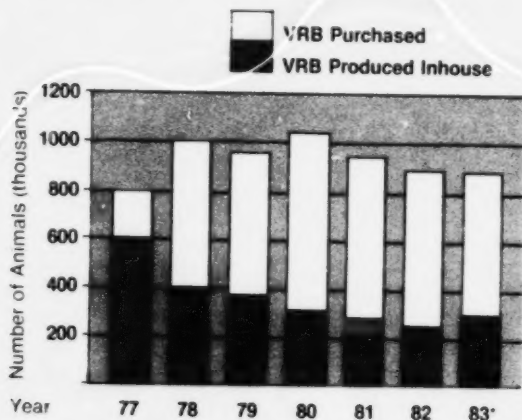
The Pathology Unit intensified its routine monitoring this year, and also responded to an outbreak of mouse hepatitis virus in the barrier-maintained colonies. Many other necropsies were performed to assist NIH investigators in distinguishing naturally occurring diseases from experimentally induced conditions. All these factors caused a 28 percent increase in the number of necropsies performed by the Unit.

Changes in methods used to monitor animal health have improved efficiency and resulted in a 17 percent decrease in the number of samples required. The number of samples processed by the Microbiology Unit increased slightly, however, because of a greater need for microbiologic investigations in connection with diagnostic pathology.

Intramural researchers' use of the Animal Disease Investigation Service declined by 13 percent during the year; the decrease is thought to reflect overall reductions in the use of laboratory animals.

Genetic monitoring of inbred mice and rats from the colonies of the NIH Animal Genetic Resource increased: rodents monitored from the foundation colony increased in number from 758 to 808, and in the pedigreed expansion colony from 62 to 143. Genetic contamination was found in a VRB foundation colony of BALB/c nude congenic mice (BALB/cAnN-nu), but no animals have ever been issued from this colony. Back-crossing is under way in the Small Animal Section to make this congenic strain available from VRB. The Genetics Unit also conducted two major investigations of genetic contamination in inbred mice received from contractors. The number of requests from NIH components for investigations of genetic problems was stable at 25.

Figure 6.
Small Animals Issued



Veterinary Medicine and Surgery Section

The professional staff of the Veterinary Medicine and Surgery Section interacts with NIH investigators in defining and developing animal models to best meet intramural research program needs. During the past year, the section assisted in implementing 23 new studies involving its animals and facilities.

The Surgery Unit provides central animal radiological and surgical facilities to NIH investigators. The Comparative Medicine Unit works closely with the surgical staff both to provide comprehensive veterinary services for the care of animals and to meet research protocol needs.

The Primate Research Unit provides research holding for more than 1200 nonhuman primates assigned to investigators representing most of the NIH institutes. The demand for central holding space remained high, and the section is continuing to issue animals from one study to another through its primate recycle program—a cost-saving feature as well as an effort to conserve nonhuman primates.

Timed-pregnant primates are used by the National Institute of Child Health and Human Development and the National Institute of Neurological and Communicative Diseases and Stroke for studies in a number of areas include birth defects and fetal effects of infectious diseases. Investigators used fewer timed-pregnant primates this year because of program changes in the institutes, resulting primarily from budget restrictions. The section terminated the contract source of these animals and can now meet investigators' needs from its inhouse colony of timed-pregnant rhesus and cynomolgus monkeys.

Interagency Primate Steering Committee

The Interagency Primate Steering Committee (IPSC) prepared a report updating the National Primate Plan, which was published in 1978. The IPSC represents the combined interests of Federal agencies in the supply, use, and conservation of nonhuman primates for many essential health activities, especially biomedical research and testing. The National Primate Plan was prepared to ensure adequate supplies of these irreplaceable animals.

The new report reviews current requirements for nonhuman primates to meet health needs.

Regarding importation and domestic breeding, it makes specific recommendations which reflect the overall decline in the use of these species. The reduced utilization appears to result from increasing costs for animals, budgetary constraints, the substitution of other species or methods, and the application of recommendations in the National Primate Plan to use these animals only when necessary and then in the most effective manner, including sharing among users.

The IPSC also sponsored a task force meeting to develop recommendations for preserving and maintaining chimpanzees used in research, and it has supported the development of a handbook, *Behavior and Management of Chimpanzees in Captivity*.

Programs to assist interested Latin American, Asian, and African countries in the breeding and conservation of indigenous species were continued through the Pan American Health Organization (PAHO) and the World Health Organization (WHO). The Committee also reviewed a draft convention of the Council of Europe on the protection of experimental animals and drafted the Federal Government's response to an inquiry from the Council about the possibility of the United States becoming a signatory to the convention.

Guidelines for the transportation of nonhuman primates were developed by the IPSC and recommended for adoption by Federal agencies and other organizations that need to transport these animals.

Outlook for 1983

The automated data processing system at the Animal Center will be expanded to include the capability to bill users for animals, products, and services. The lease arrangement for the Three Springs Farm, adjoining the Center, will be terminated.

The use of VRB-produced rodents is expected to increase when the Branch begins holding rodents for investigators from the National Institute of Allergy and Infectious Diseases in the recently renovated facilities in Building 14B; VRB will establish production colonies to meet these investigators' needs. In addition, many stocks and strains will be reintroduced into the barrier area to replace those that were eliminated last year to control an outbreak of mouse hepatitis virus.

The Interagency Primate Steering Committee will continue to monitor utilization of nonhuman primates and develop recommendations for meeting biomedical research needs.



Library Branch

Carolyn Brown, Chief

Coming—A Fully Automated Library System

To improve users' access to materials, the NIH Library has continued to move toward automation of all routine functions, building on the groundwork of the automated bibliographic search system and circulation control system already in place. The completed data base will reflect the Library's total holdings.

Construction of a computer room to house the new automated library system began as this fiscal year ended. Delivery of the computer is expected by April 1983. In preparation, the conversion of the Library catalog to machine-readable form was two-thirds completed at the end of the year. Files should be loaded and the online catalog activated during FY 1983. Journal control and other services will follow, including improvements in our automated circulation controls.

When the system has been installed, users will be able to browse the online catalog with touch-screen terminals similar to those used at automated banking stations. By touching various squares on the screen, the user can search the catalog by author, title, or call number. Within seconds, the screen will display the bibliographic description of any item in the collection, plus the location and circulation status of any copy of that item.

The information about each item's status will be current because the circulation control system updates the online catalog the instant it processes each loan. Online circulation control will also eliminate the current one-day delay before a change in a book's circulation status is recorded on computer, and a backup microcomputer will continue to record checkouts and returns if the main computer is temporarily down. Transactions will be recorded by the very reliable bar code system used at automated grocery checkout counters.

Another improvement in the Library's journal control system was already made this year. Information about journals received is now entered

online into the PHILSOM system (Periodical Holdings in Libraries of Schools of Medicine), a data base of journal information from a network of 19 medical libraries, including the NIH Library. The new online system can provide, on demand, lists of the Library's daily receipts, complete holdings, and skipped issues claimable from the publisher.

Yet another new online service for users in 1982 was access to the Library's Monthly Acquisitions List, now available through WYLBUR, the computer system maintained by the NIH Division of Computer Research and Technology. Regular printed copies of the monthly list continue to be available to the Library's users as well.

Computerized Bibliographic Retrieval Services

Another of the Library's automated services—computerized bibliographic retrieval—continued to occupy a high percentage of the workload in the Reference and Bibliographic Services Section. As prices rose for searching many of the online files, it became necessary to reduce searches of the pre-1975 literature; most investigators were satisfied by citations from the more current literature. The number of searches remained approximately constant because of almost level funding and a careful effort to conserve funds.

A study of users' satisfaction with the Library's online search services was made this year by a student in the University of Maryland's Graduate School of Library and Information Services. The staff was happy to learn that 87 percent of the 295 respondents in the survey rated the search interview "very satisfactory," and 88.3 percent judged the search results to be either "of major value" or "of considerable value." Many of the respondents also praised the turn-around time.

Journals and Books—Solving the Space Problem

The growth of the NIH Library's holdings through the years has resulted in insufficient shelf space. As lack of space became acute, the Library began weeding the 6,000 titles in the journal collection, starting with a review of 900 journals that have either ceased publication or been discontinued by the Library. This year the weeding of the journal collection continued, and a similar review of the book collection was begun. The selection and review of material proposed for removal from the shelves has involved all sections of the Library as well as the Library Advisory Committee and interested NIH staff. The project will continue throughout FY 1983.

The Library's actions to relieve space problems were hampered somewhat by the Government-wide freeze on hiring, which caused lengthy vacancies in several positions most involved in decisions on removing material from the collection. Among these vacancies were the positions of Library Chief, Deputy Chief, and Section Chief for Reference and Bibliographic Services.

Readers Services Section

In a continuing effort to upgrade and update the Library's photocopying facilities, the Readers Services Section has replaced older equipment with newer machines, after placing several trial models in our user area and obtaining users' comments on them.

Services of the NIH Library

The NIH Library offers a full array of services to assist scientific investigators in their work. They include:

- **Computer Bibliographic Services** - Six specialists perform computerized literature searches and compile bibliographics upon request. The staff is experienced in retrieving citations and abstracts from some 155 scientific data bases.
- **Current Awareness Service** - The Library's Selective Dissemination of Information (SDI) program provides users with regular computer updates on new literature in any specified subject area.
- **Reference Services** - Reference librarians not only answer reference questions on site or by telephone (496-2184), but also advise users of other library services that may meet their needs.
- **Photocopying** - High speed photocopying machines are available to users. The Library also fulfills copying requests.
- **Microfilm and Microfiche** - Many journals are also kept in microform. Most are backfiles of important titles, acquired in order to save space. Reader-printers are located nearby.
- **Circulation** - Books other than reference works can be checked out. Second copies of certain journals are also available for circulation.
- **Interlibrary Loans** - Research publications not in the collection can be obtained from other libraries. Photocopies of journal articles obtained from the National Library of Medicine are usually provided in one to three workdays.
- **Translations** - Foreign language scientific materials are translated at request, and the translations are made available to other users as well.
- **Stack Service** - Library staff will search for any volume a user cannot find on the shelves.
- **Monthly Acquisitions List** - This list, "Recent Additions to the NIH Library," is available in printed form and on the NIH WYLBUR computer system.
- **Library Tours** - A tour with explanations of NIH Library services and policies is available every Wednesday at 2 p.m.
- **Carrels** - Private study carrels are available on limited, first-come basis.